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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,583	04/09/2004	Yan Wang	020130-000112US	1973

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
05/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,583	WANG ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/04;3/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are at issue and are present for examination.

Applicant's election of species 2, a method of amplifying a target nucleic acid using a protein comprising a domain that is bound by a polyclonal antibody generated against Sso7d, in the paper of 2/12/2007, is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure statements filed on 4/9/2004 and 3/7/2007 are acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities: Applicants state that the instant application is a continuation of parent application No. 09/870,353, however, it appears that this application is more accurately referred to as a divisional.

Appropriate correction is required.

Claim Objections

Claims 5 and12 are objected to because of the following informalities:

Claims 5 and 12 each recite "Sso7D" while the rest of the claims and applicants specification recite "Sso7d". It is suggested that applicants maintain consistency throughout the application.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 3, 9 and 10 recite the limitation "nucleic-acid-modifying domain" in claims 1 and 8, respectively. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-14 are directed to all possible methods of amplifying a target nucleic acid comprising contacting the target nucleic acid with a protein comprising at least two heterologous domains, wherein a first domain that is a sequence-non-specific nucleic-acid-binding domain is joined to a second domain that is a polymerase domain with error-correcting activity, wherein the sequence non-specific nucleic-acid-binding domain: a) binds to double-stranded nucleic acid and b) enhances the processivity of the polymerase compared to an identical polymerase not having the sequence non-specific nucleic-acid binding domain fused to it, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain.

The specification, however, only provides the representative species of methods of amplifying a target nucleic acid, comprising the use of a Sso7d-delta*Taq*, Sso7d-*Taq*, and *Pfu*-Sso7d fusion proteins encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species with respect to those sequence-non-specific nucleic acid binding domains which are capable of enhancing the processivity of an attached DNA polymerase domain beyond the full-length Sso7d protein as well as those polymerase domains which are amenable to having their processivity increased by such a mechanism. Given this lack of additional representative species as encompassed by the claims, applicants have failed to

sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those methods of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains, wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain is Sso7d, does not reasonably provide enablement for any method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-14 are so broad as to encompass any method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins, specifically sequence-non-specific-double-stranded nucleic–acid-binding domains, broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place in sufficient structural limits on the claimed sequence-non-specific-nucleic–acid-binding domains as well as those polymerase domains which are amenable to having their processivity increased by such a mechanism. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a

protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited those representative species of Sso7d-delta*Taq*, Sso7d-*Taq*, *Pfu*-Sso7d and Sac7d-delta*Taq* encompassed by these claims.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass those methods of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA

polymerase domain, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the sequence-non-specific-nucleic–acid-binding activity; (B) the general tolerance of the domains to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of said domains with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain function claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having the claimed activities.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein

said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those proteins and methods of their use having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-19, 21, 22 and 25 of copending Application No. 10/306,827. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-12, 14-

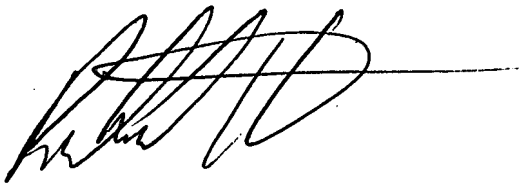
19, 21, 22 and 25 of 10/306,827 drawn to a method of increasing the yield of from a polymerase reaction on a target sequence comprising contacting the target nucleic acid with a polymerase joined to a sequence non-specific-nucleic –acid-binding domain anticipate claims 1-14 drawn to a method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
5/8/2007